



UNITED STATES PATENT AND TRADEMARK OFFICE

EA

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/894,423 | 06/28/2001 | Ronald H. Chiarello | SYNGEN-06067 | 6875 |

23535 7590 06/29/2005

MEDLEN & CARROLL, LLP
101 HOWARD STREET
SUITE 350
SAN FRANCISCO, CA 94105

| |
|----------|
| EXAMINER |
|----------|

QIAN, CELINE X

| | |
|----------|--------------|
| ART UNIT | PAPER NUMBER |
|----------|--------------|

1636

DATE MAILED: 06/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/894,423

Applicant(s)

CHIARELLO ET AL.

Examiner

Celine X. Qian Ph.D.

Art Unit

1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 April 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 4 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 4 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 6/28/01, 4/7/03 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>12/22/03, 1/12/04</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1 and 4 are pending in the application.

This Office Action is in response to the Amendment filed on 4/19/05.

Response to Amendment

The rejection of claims 1 and 4 under 35 U.S.C. 112 1st paragraph is maintained for reasons set forth of the record mailed on 11/15/04 and further discussed below.

The rejection of claims 1 and 4 under 35 U.S.C. 102 (e) is maintained for reasons set forth of the record mailed on 11/15/05 and further discussed below.

Response to Arguments

Claim Rejections - 35 USC § 112

Claims 1 and 4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In response to this rejection, Applicants argue that the specification provides sufficient description for the claimed genus of bifunctional linker arm. Applicants point to the teaching in the specification which defines the term “bifunctional linker” as a compound that can link two additional compounds together by chemically interacting with both of them simultaneously, and gives an example of such a compound. Applicants also cite the disclosure in the General Description section, “Following activation of the carboxyl functional group... Such a linker arm serves several functions. It provides needed distance between the label and the oligonucleotide,

Art Unit: 1636

a functional group, in this case an amine...in this case a hydroxyl, which will ultimately allow for the coupling to the 5' hydroxyl of a support-bound protected oligonucleotide." Applicants assert that such descriptions fully describe the essential structure of said bifunctional linker that is responsible for a bifunctional linker. Further, Applicants argue that the amended claims now recite the structure of the bifunctional linker comprises a "hydrocarbon chain," which is demonstrated in Table 1, 2, 3 and Figures 1A-B, 2A-B, 3-5 of the application. Applicants assert that a representative number of species of bifunctional linker arms is thus described in said drawings and tables. Applicants thus conclude that the written description requirement is satisfied.

The above arguments have been fully considered but deemed unpersuasive. The detailed reasons for lack of description of the claimed bifunctional linker were discussed in detail in the previous office action. In response to Applicant's argument, Applicant is reminded that the claimed genus of bifunctional linker encompasses potentially a large genus of compounds which comprise a hydrocarbon chain of varying length (1 to infinite length) or structure (i.e., straight, branch, or cyclic), a protected secondary amine, and a hydroxyl group. This claimed genus comprises a large number of species of compounds may have function that is unrelated to bifunctional linker, and unrelated to each other. The paragraphs cited by Applicants describe the functional aspects of said bifunctional linker, but not the complete structure for the claimed genus of bifunctional linker. It is well known in the art that the function of a chemical compound is determined by its complete structure, not by a single group. As such, the function of the bifunctional linker such as "providing the needed distance" and "linking the support bound oligonucleotide and the label" is determined by the complete structure of the bifunctional linker,

Art Unit: 1636

not any compound that comprises a protected secondary amine, a hydroxyl group and a hydrocarbon chain of any kind. The specification only discloses a phosphoramidite bifunctional linker. The linker compound listed in Tables 1, 2, 3 has almost the same structure (the linker in Table 1 only differs in the length of carbon chain from 1 to 5), which is a phosphoramidite bifunctional linker. There is no other chemical structure of a bifunctional linker depicted in Figures 1-5 except the phosphoramidite bifunctional linker in Figure 2A (which is same as those listed in Tables 2-3). In view of the huge genus as claimed, the disclosure of a phosphoramidite bifunctional linker does not constitute a representative number of species for this vast genus, thus the specification fails to describe the complete structure for the claimed genus of compounds. Although the specification describes the function of the bifunctional linker, the structural and functional relationship between the claimed compounds and function is missing. Therefore, the written description requirement is not met. This rejection is thus maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1 and 4 are rejected under 35 U.S.C. 102(e) as being anticipated by Vinayak (US 6,255,476).

In response to this rejection, Applicants argue this reference is previously cited and withdrawn in view of Applicants' rebuttal. Applicants assert that the Examiner should not

Art Unit: 1636

reapply this reference according to the guidance given in MPEP to avoid piecemeal examination and undue multiplication of references. Applicants further assert that Vinayak et al. do not anticipate the instant claims because this reference is silent on an unactivated label which is subsequently reacted, *in situ*, to form an activated label. Applicants cited a paragraph from Vinayak stating “a pre-activated label is covalently attached to 5 to yield the labeled support 6” to demonstrate that the activation of the label does not occur *in situ*. Applicants assert that the present invention as disclosed in Figure 3 describes an “in situ-produced activated TMR,” and this limitation is not taught by Vinayak et al. Applicants thus conclude Vinayak et al. fail to describe every element of the claimed invention, and the rejection should be withdrawn.

The above arguments have been fully considered but deemed unpersuasive. The claims are anticipated by Vinayak et al. for reason set forth of the record mailed on 11/15/05. In response to Applicants’ argument with regard to reapplication of the Vinayak reference, the Examiner directs Applicants’ attention to the claims filed on 4/7/03 and the office action mailed on 6/17/03. Clearly as stated in the office action mailed on 6/17/03 (see page 2), the rejection is withdrawn because Applicants amendment of the claims (see claims filed on 4/7/03), not because Applicant’s successful rebuttal of the art. However, in the response filed on 12/22/03, Applicants amended the claims to the current scope, wherein the reference anticipates the claims. As such, the examiner did not ignore the guideline from MPEP, the reapplication of the reference is solely based on Applicants’ amendment of the claims, which is not against any rules set forth by MPEP.

In response to Applicants’ argument with regard to *in situ* activation, Applicants is reminded that such limitation needs to be interpreted in the context of the claims in view of the

Art Unit: 1636

art. The specification does not define “*in situ* activated/unactivated label,” wherein it is unclear how to interpret “*in situ* reaction” in the context of a chemical reaction where it does not occur in a cell or organism. The Webster dictionary interprets this term as “in position, in the natural or original position or place.” However, in the context of the claims 1 and 4, it is unclear what is this natural or original position of the label. Figure 3 does not illustrate this “natural or original position” of the label either. As such, the step c) of claims 1 and 4 is interpreted as an unactivated label being activated by certain means and such activation occurs before the label reacts with the support bound linker-oligonucleotide. The term “pre-activated label” in col. 9 of Vinayak et al. still anticipates the claims because it simply means that the label is activated before it reacts with the support linker. Furthermore, Vinayak et al. also disclose that “prior or separate activation/pre-activation of a label functionality is not necessary to the practice of the present invention,” which means the activation can occur simultaneously with the labeling reaction in the presence of coupling agent such as HBTU (see Figure 7, and 13, 2nd paragraph). As such, if the *in situ* activation as claimed means the activation of label and reaction with support bound linker occurs at same position, the Vinayak reference still anticipates the claims. Therefore, for reasons set forth in the previous office action and above, this rejection is maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

Art Unit: 1636

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X. Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CELIAN QIAN
PATENT EXAMINER



Celine X Qian Ph.D.
Examiner
Art Unit 1636